

A.L.B.U.M.S: ALDEHYDE - LINKER - BASED
ULTRASENSITIVE MISMATCH SCANNING.

1. ISOLATE mRNA FROM CANCEROUS AND NORMAL TISSUE.
GENERATE cDNA LIBRARY FOR GENES TO BE SCREENED.

2. A MIX, HYBRIDIZE C
MUTATION WILD TYPE



A/G MISMATCH (25%)

3. TREAT w. MISMATCH REPAIR GLYCOSYLASES.
LABEL RESULTING ALDEHYDES w. FARP.
IMMOBILIZE FARP - LABELED DNA ON MICROPLATES.

4. DETECT TOTAL MUTATION VIA CHEMILUMINESCENCE.
ISOLATE AND RECOVER MUTATED DNA, PCR.
IDENTIFY MUTATION - CONTAINING GENES
ON DNA ARRAYS FOR HUNDREDS/THOUSANDS OF GENES.

└─> VERIFY BY
SEQUENCING

ESTABLISH SINGLE-STEP SCREENING OF HUNDREDS OR
THOUSANDS OF GENES IN CANCER SAMPLES FOR MUTATIONS.
STREAMLINE AND DISSEMINATE THE TECHNOLOGY.

FIG. 1

TECHNOLOGY FOR ISOLATING AND IDENTIFYING MUTATIONS
OVER HUNDREDS OR THOUSANDS OF GENES SIMULTANEOUSLY:
AN EXAMPLE OF SCREENING FOR A-TO-C TRANSVERSIONS.

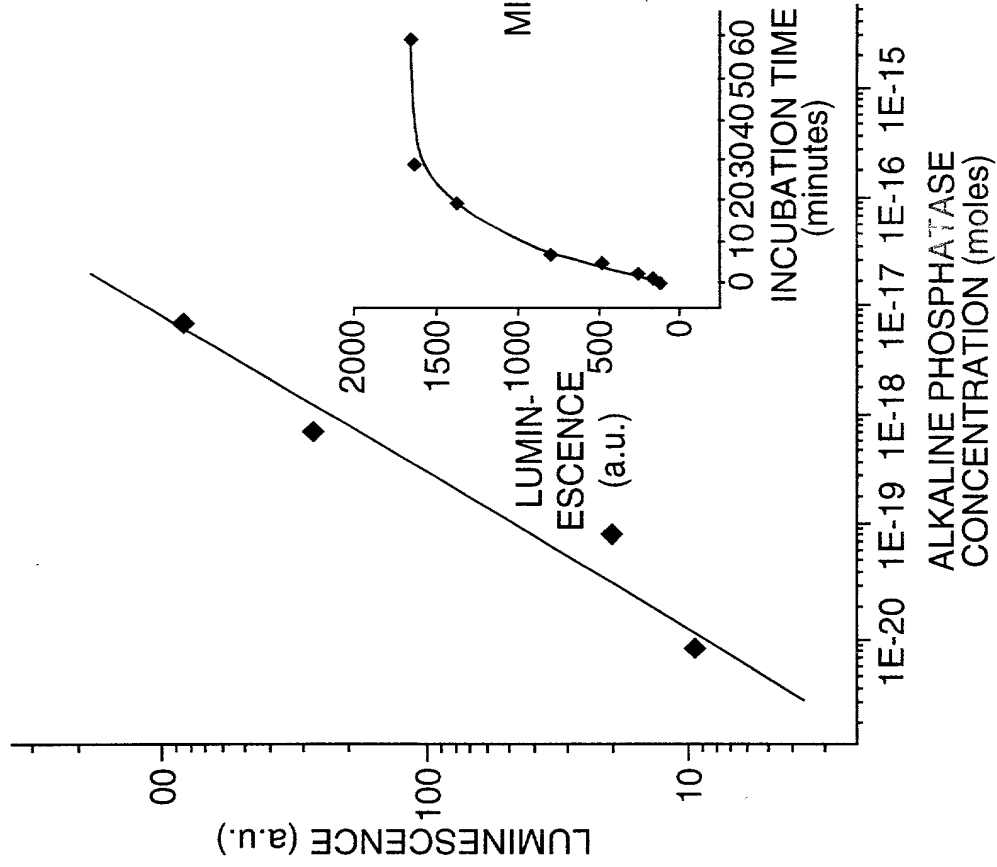


FIG. 2A

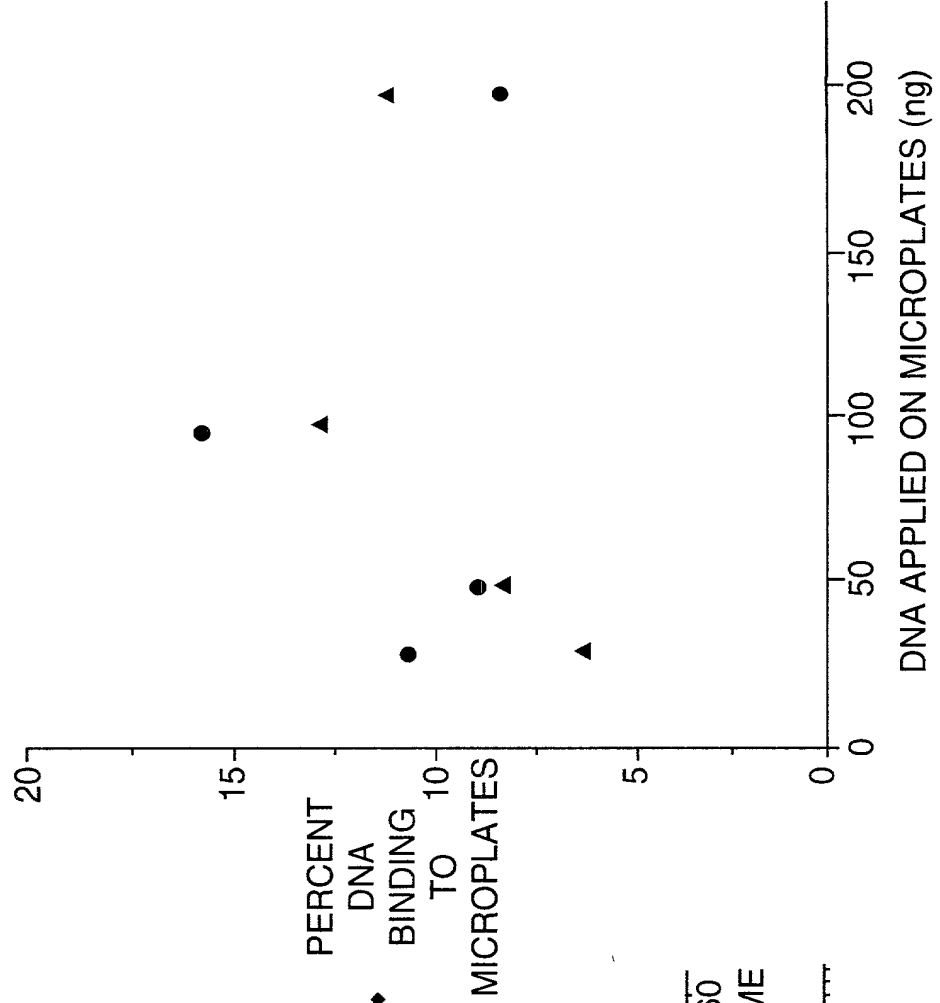


FIG. 2B

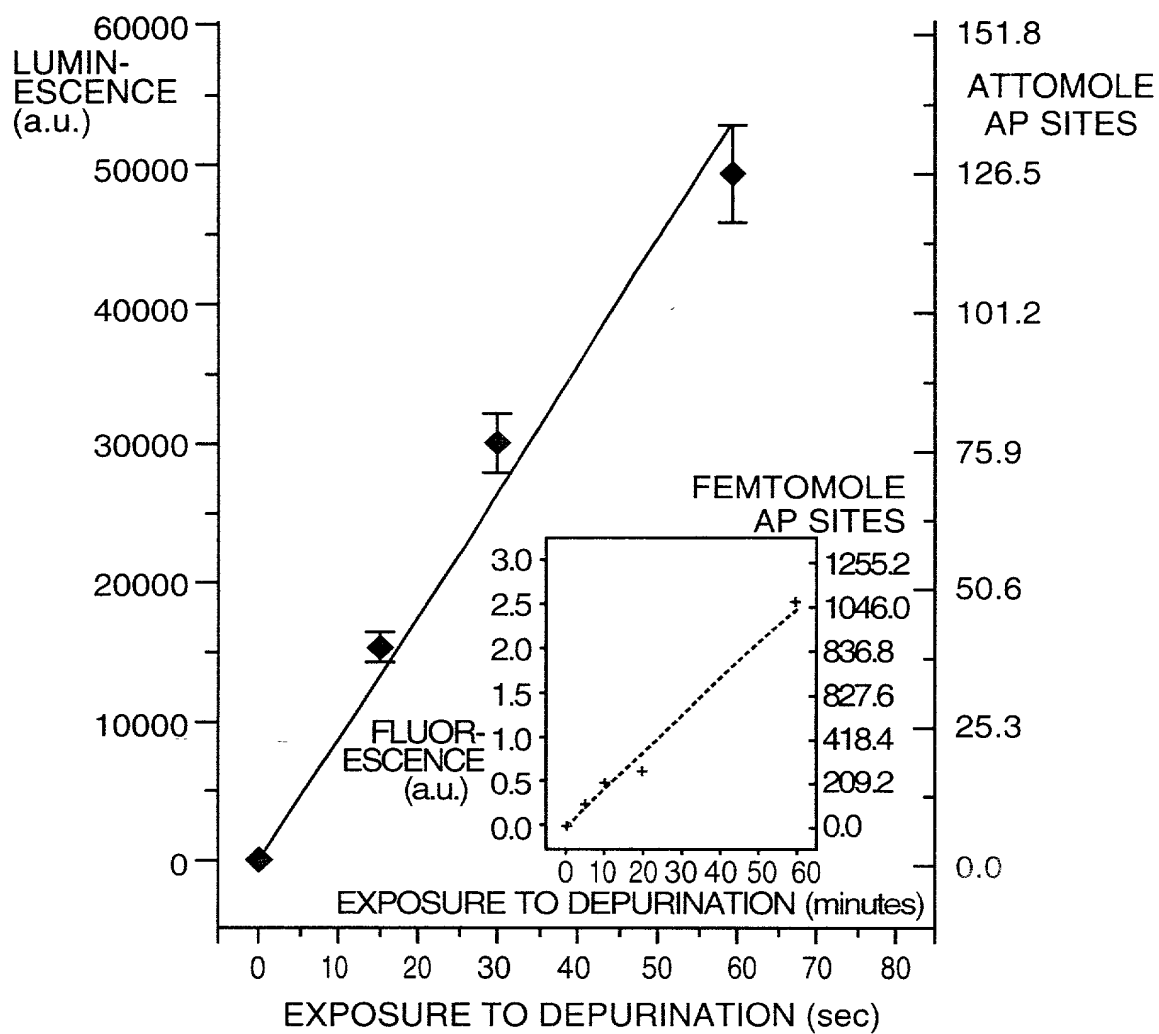


FIG. 3

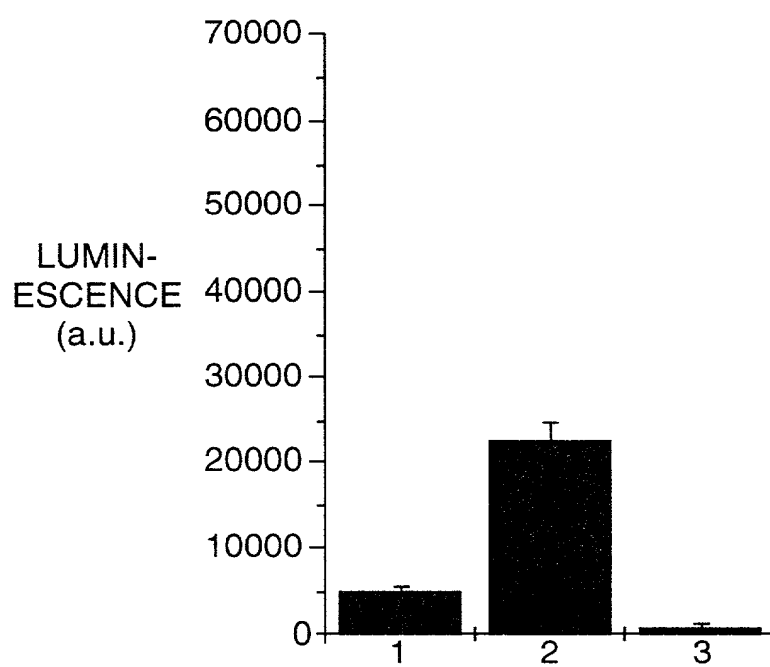


FIG. 4A

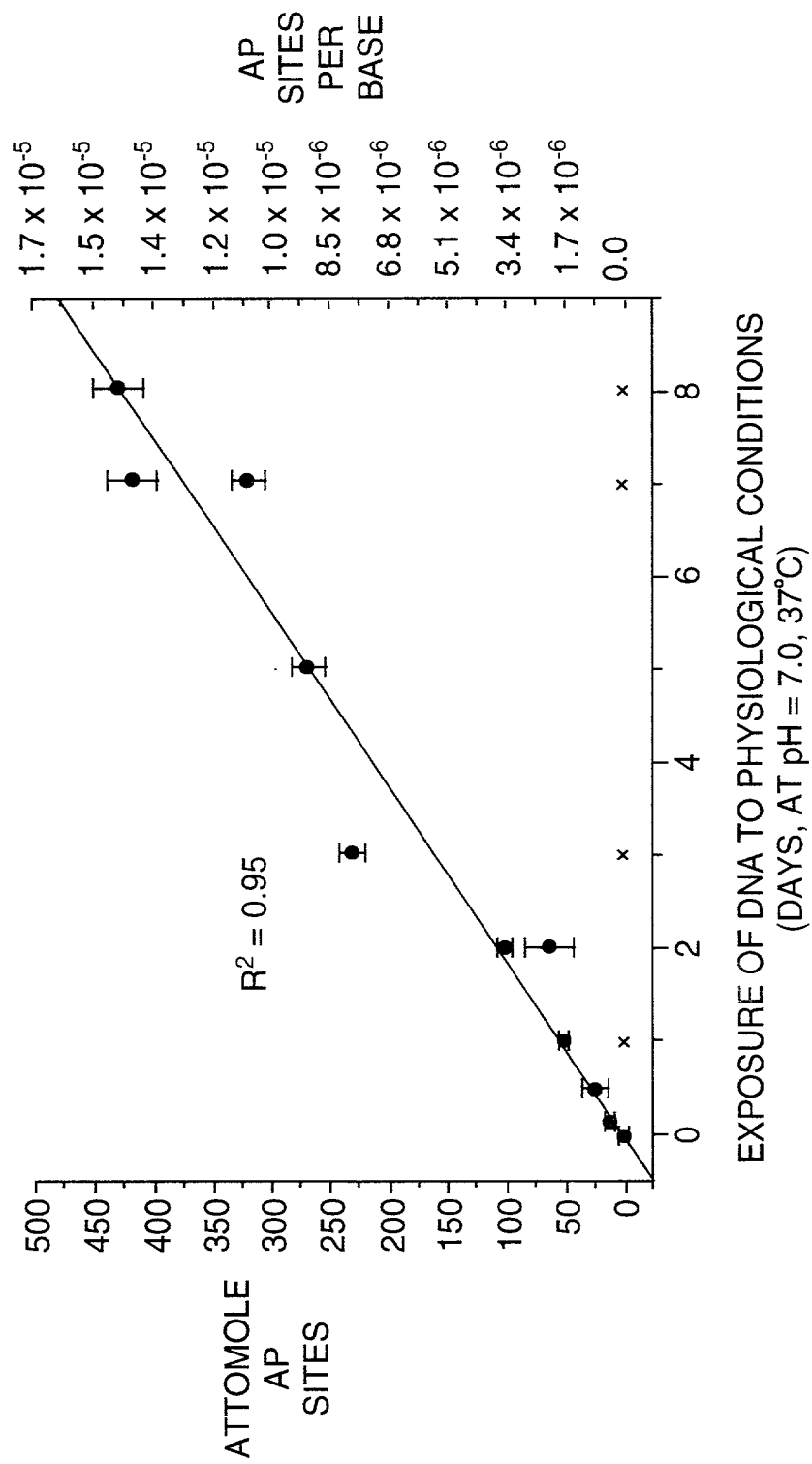


FIG. 4B

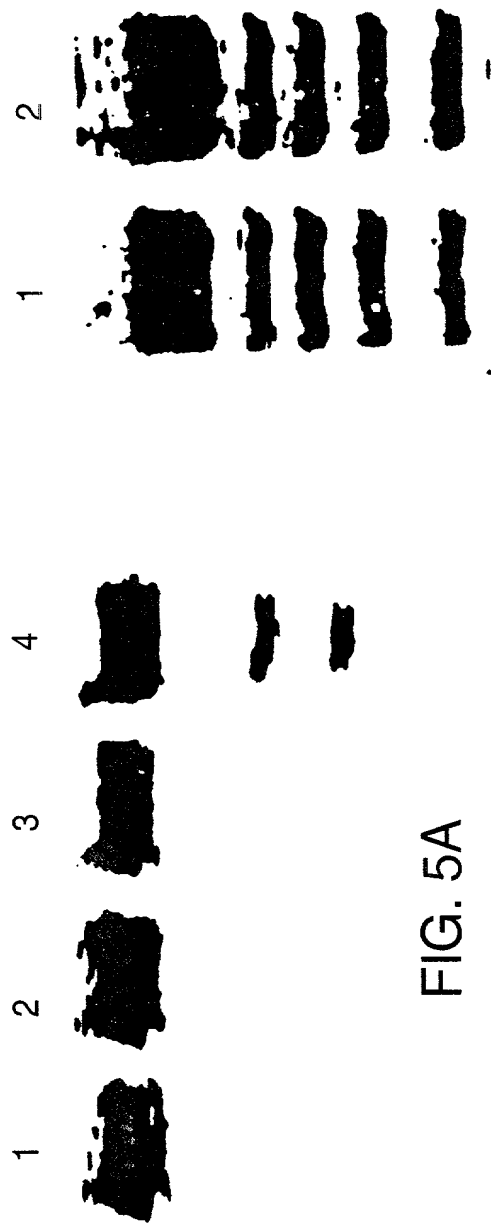


FIG. 5A

FIG. 5B

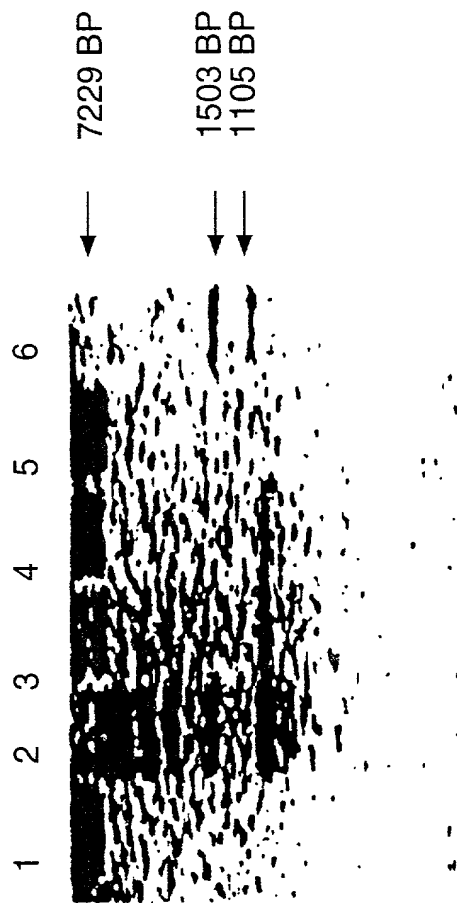


FIG. 5C

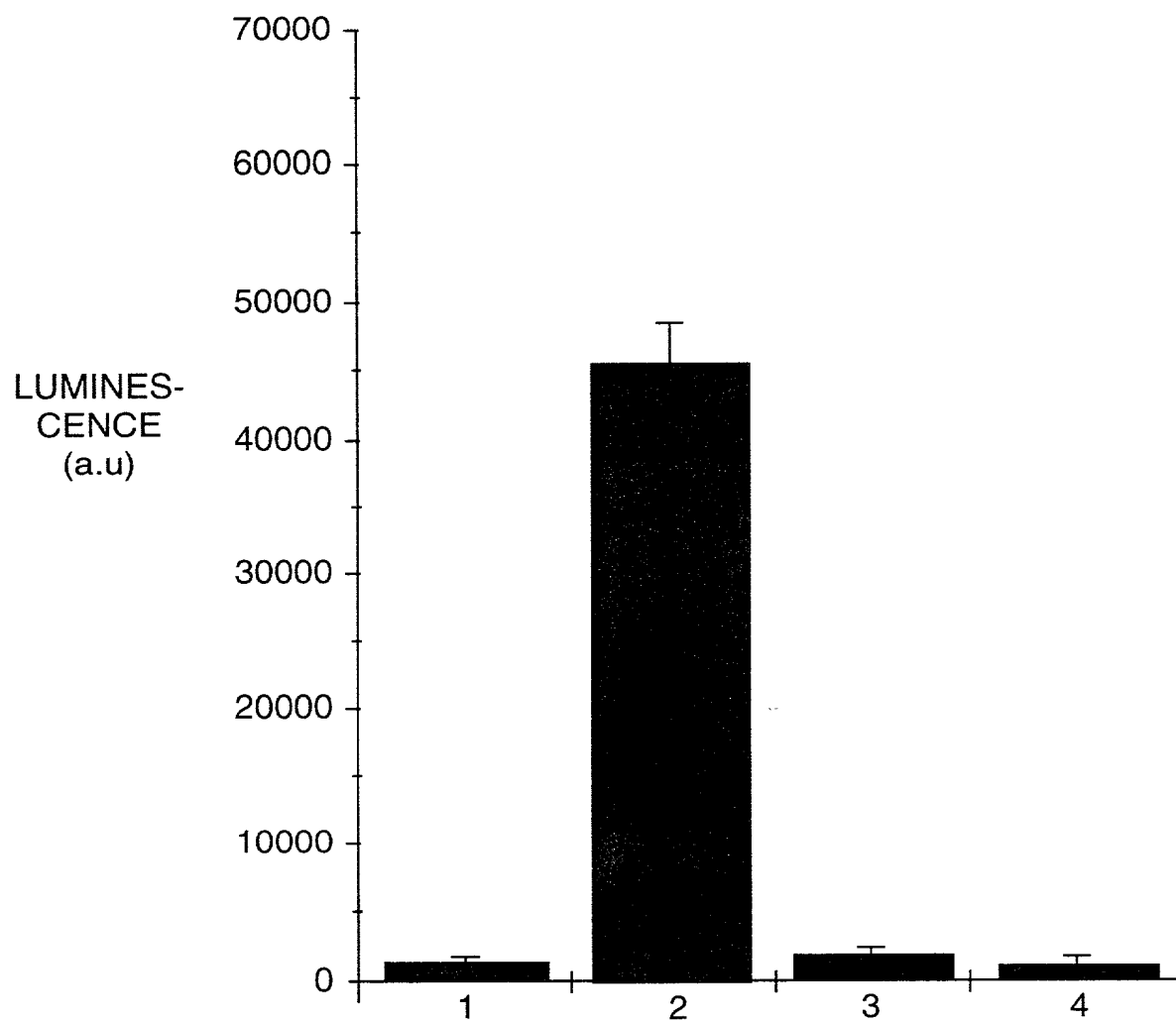
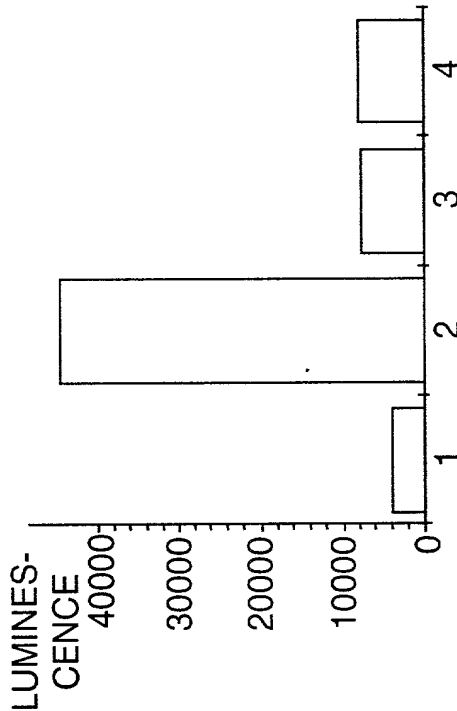


FIG. 6

Condition	Luminescence (a.u.)
1	~500
2	~29,500
3	~500
4	~500

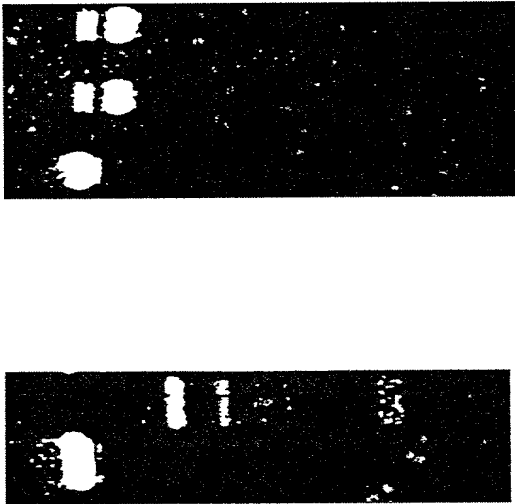
FIG. 7

DETECTION OF MISMATCHES FORMED BY
HYBRIDIZING OLIGONUCLEOTIDES WITH M13 DNA
AND EXPOSED TO MutY ENZYME



- 1= S.S. M13 DNA WITH ~ 1 A/G MISMATCH PER 2500 BASES, NO ENZYME
- 2= S.S. M13 DNA WITH ~ 1 A/G MISMATCH PER 2500 BASES, NO ENZYME
- 3= D.S. M13 DNA WITHOUT MISMATCH, NO ENZYME
- 4= D.S. M13 DNA WITHOUT MISMATCH, PLUS ENZYME

FIG. 8A



- 1= SINGLE STRANDED (S.S) M13 WITH 1 A/G MISMATCH PER 2500 BASES, NO ENZYME
- 2= S.S. M13 WITH 1 A/G MISMATCH PER 2500 BASES. PLUS ENZYME
- 3= S.S. M13 WITH 1 A/G MISMATCH PER 2500 BASES, NO ENZYME
- 4= DOUBLE STRANDED M13 WITHOUT MISMATCH, NO ENZYME
- 5= D.S. M13 WITHOUT MISMATCH, PLUS ENZYME

FIG. 8B

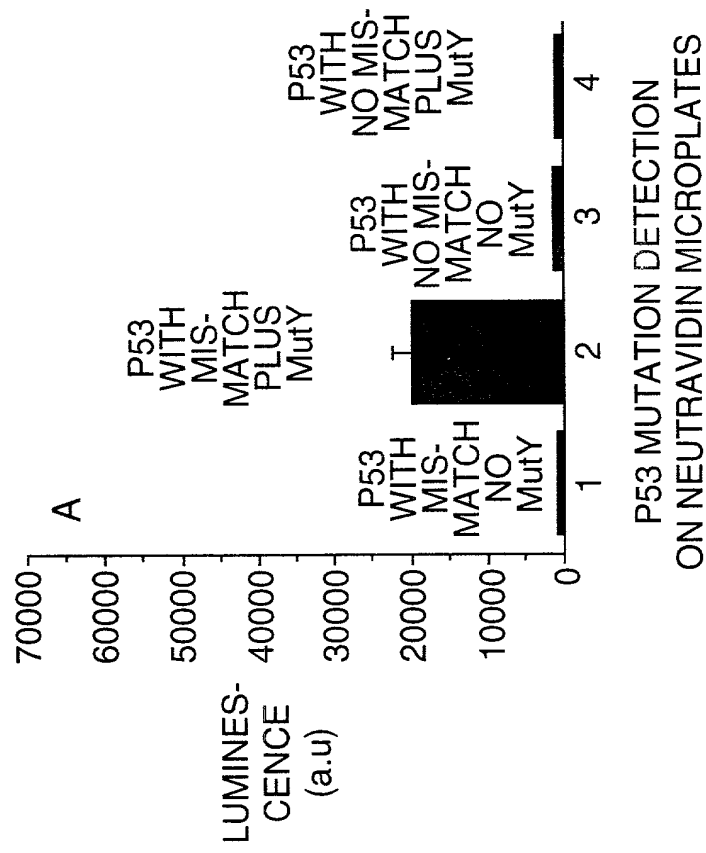
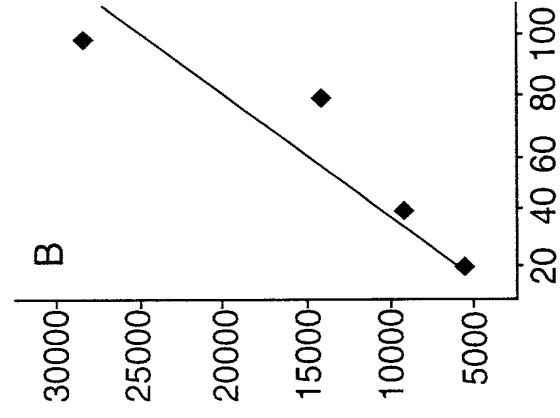


FIG. 9A



AMOUNT OF P53 SAMPLE APPLIED
ON NEUTRAVIDIN MICROPLATES (ng)

FIG. 9B

M13mp19 DNA TESTED.

A = DNA ALONE

B = DNA PLUS MUTY

C = DNA PLUS 5mM METHOXYAMINE PLUS MUTY

D = DNA PLUS 5mM AED PLUS MUTY

E = DNA PLUS 10mM AED PLUS MUTY

F = DNA PLUS 5mM BARP PLUS MUTY

F E D C B A

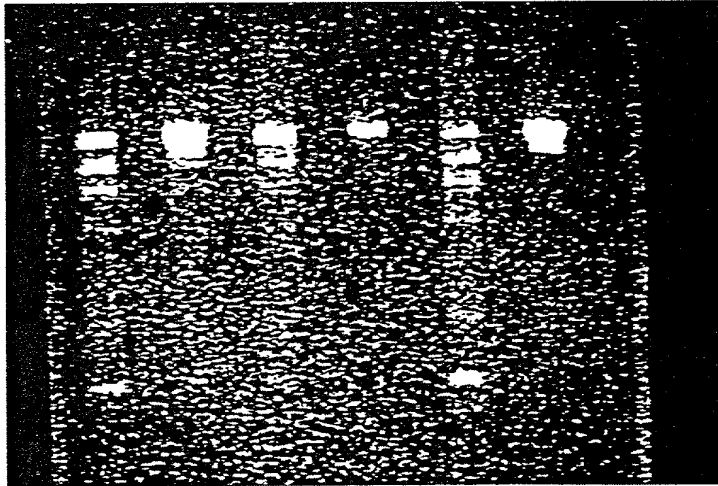


FIG. 10A

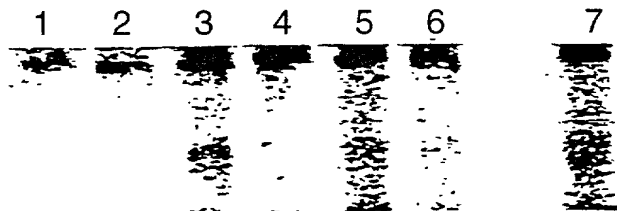


FIG. 10B

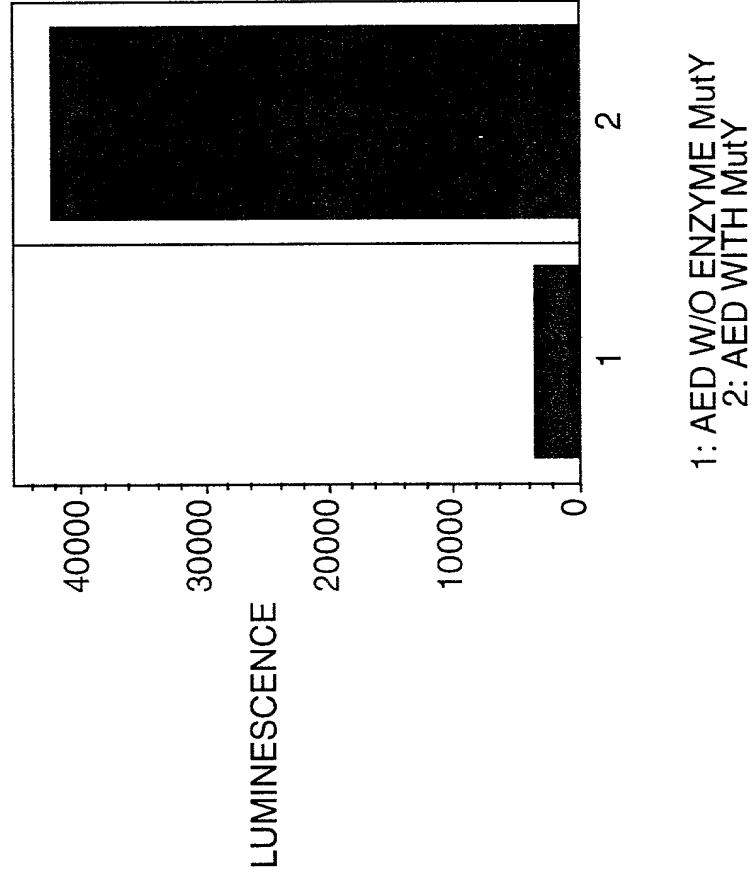


FIG. 11

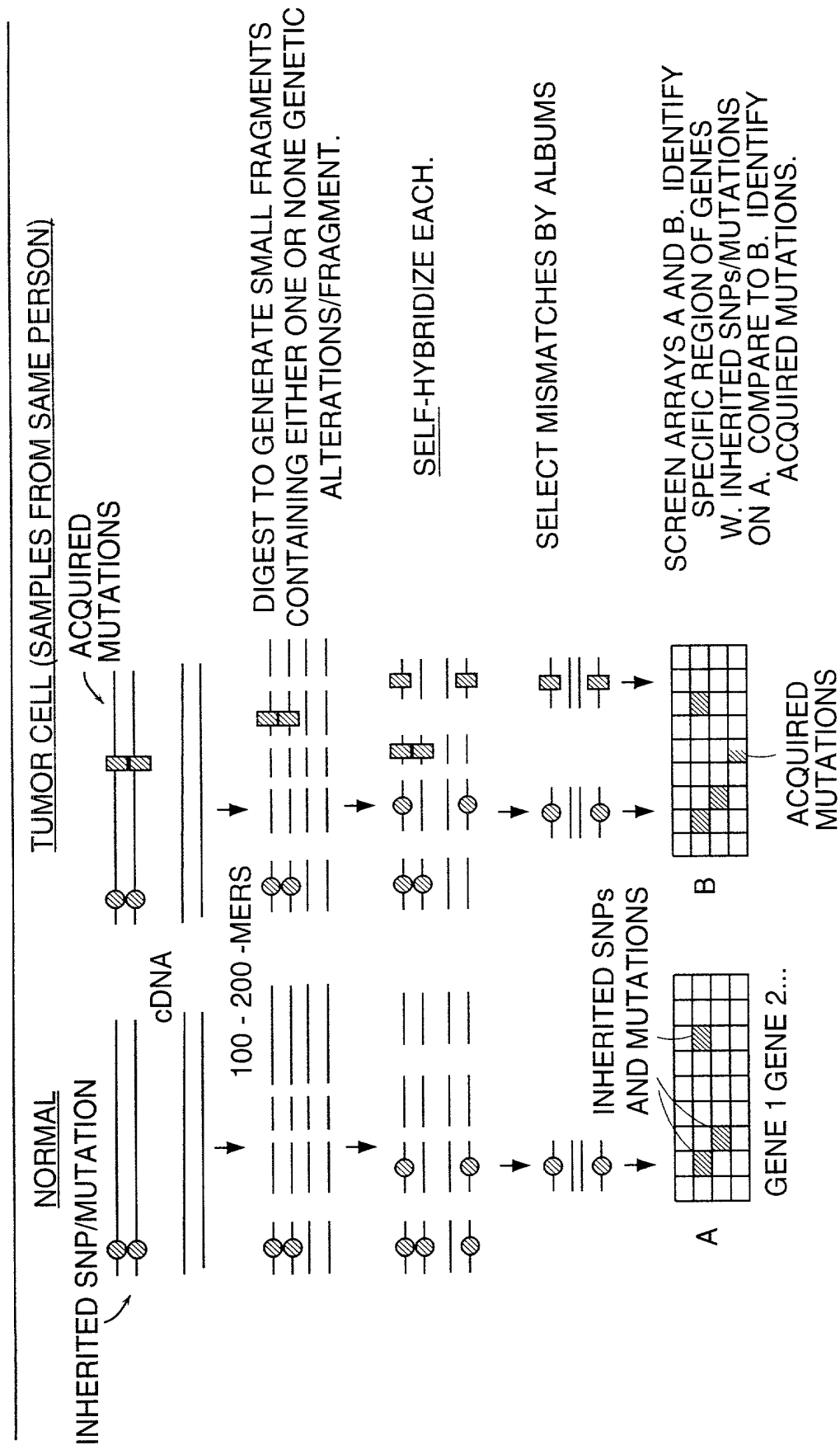


FIGURE 12

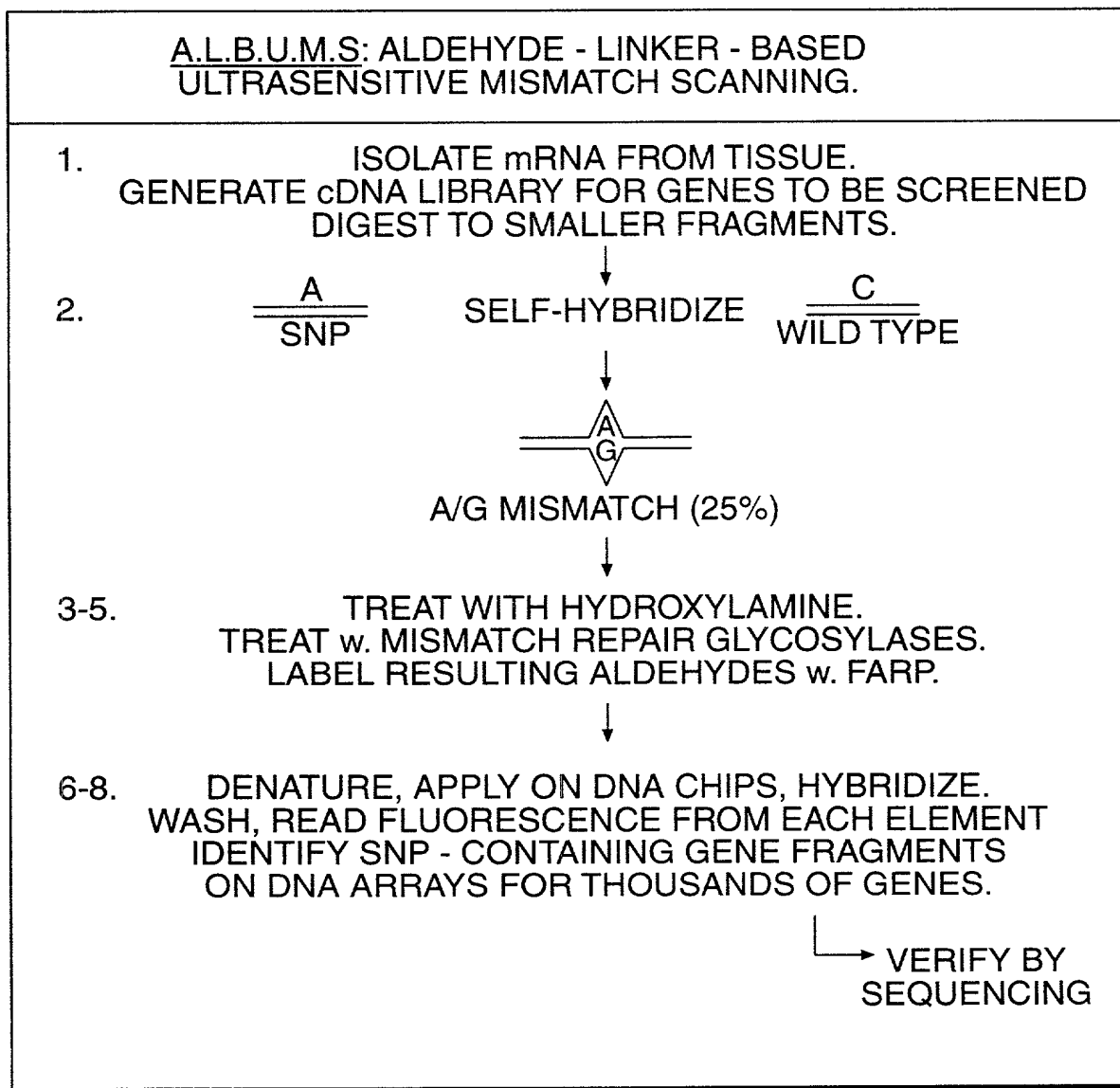


FIG. 13

SIMPLIFIED PROTOCOL TO DETECT SNPs
AND MUTATIONS ON DNA CHIPS.

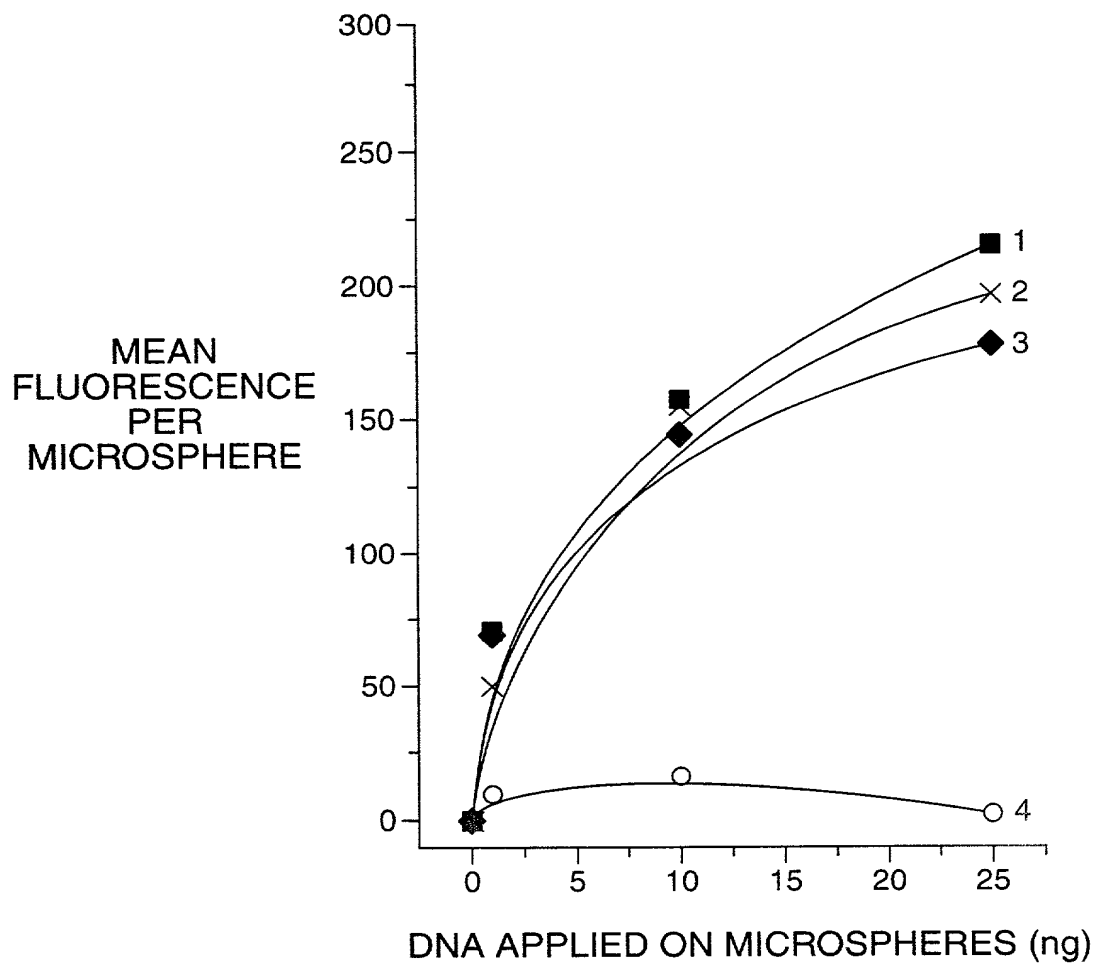


FIG. 14

MICROSPHERE-BASED MUTATION SCANNING ARRAYS

EACH CODING SEQUENCE IS REPRESENTED BY
OLIGONUCLEOTIDES (■) SAMPLING THE mRNA
AT REGULAR INTERVALS.

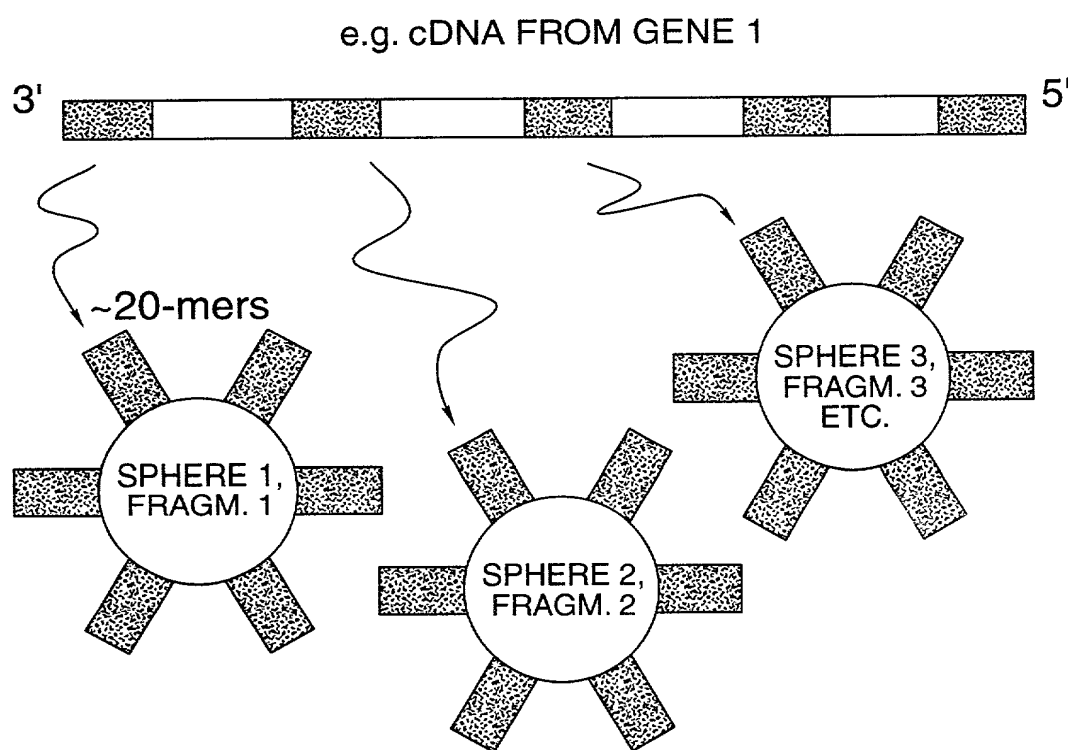


FIG. 15

THE OUTPUT INFO IS IN BINARY FORMAT